International Application No PCT/US2004/019229

		PC1/US200	4/019229
A. CLASSIF IPC 7	C12N15/11 A61K31/7088 A61K48/00		
According to	. International Patent Classification (IPC) or to both national classification	n and IPC	<u> </u>
B. FIELDS	SEARCHED		
Minimum do IPC 7	cumentation searched (classification system followed by classification s ${\sf C12N-A61K}$	symbols)	
	ion searched other than minimum documentation to the extent that such		
Electronic da	ata base consulted during the international search (name of data base	and, where practical, search terms used	
EPO-In	ternal, Sequence Search		
C. DOCUME	ENTS CONSIDERED TO BE RELEVANT		
Category °	Citation of document, with indication, where appropriate, of the relevant	ant passages	Relevant to claim No.
Х	US 6 518 417 B1 (SCZAKIEL GEORG AN VOLKER) 11 February 2003 (2003-02-	ND PATZEL -11)	21,24, 25,27, 30,31
Y	the whole document		1-4, 13-15,20
	column 2, lines 15-22; sequences column 4, lines 51-56	4-121	
Y	HOLEN T ET AL: "Similar behavious single-strand and double-strand suggests they act through a commo pathway" NUCLEIC ACIDS RESEARCH, OXFORD UN PRESS, SURREY, GB, vol. 31, no. 9, 1 May 2003 (2003-pages 2401-2407, XP002281439 ISSN: 0305-1048	iRNAs n RNAi IVERSITY	1-4, 13-15,20
	the whole document		
		/	
X Fur	ther documents are listed in the continuation of box C.	X Patent family members are listed	I in annex.
° Special ca "A" docum consist "E" earlier filing "L" docum which citatic "O" docum other "P" docum	ent defining the general state of the art which is not dered to be of particular relevance document but published on or after the international date ent which may throw doubts on priority claim(s) or is cited to establish the publication date of another on or other special reason (as specified) sent referring to an oral disclosure, use, exhibition or means	"T" later document published after the in or priority date and not in conflict will cited to understand the principle or invention "X" document of particular relevance; the cannot be considered novel or canninvolve an inventive step when the cannot be considered to involve an document of particular relevance; the cannot be considered to involve an document is combined with one or ments, such combination being obvin the art. "8" document member of the same pater	th the application but theory underlying the claimed invention of be considered to document is taken alone to claimed invention inventive step when the more other such docuicus to a person skilled
Date of the	actual completion of the international search	Date of mailing of the international se	earch report
17 December 2004		16. 09.	2005
Name and	mailing address of the ISA European Patent Office, P.B. 5818 Patentlaan 2 NL - 2280 HV Rijswijk Tel. (+31-70) 340-2040, Tx. 31 651 epo nl, Fax: (+31-70) 340-3016	Authorized officer Macchia, G	

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Citation of document, with indication, where appropriate, of the relevant passages GILADI H. ET AL.: "Small interfering RNA inhibits hepatitis B virus replication in mice" MOLECULAR THERAPY,	Relevant to claim No. 1,2,13, 21
GILADI H. ET AL.: "Small interfering RNA inhibits hepatitis B virus replication in mice" MOLECULAR THERAPY,	1,2,13,
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vol. 8, no. 5, November 2003 (2003-11), pages 769-776, XP008040415 siRNA-1 the whole document	
WO 03/070918 A (RIBOZYME PHARMA INC (US) MCSWIGGEN BEIGELMAN MACEJAK ZINNEN PAVCO ET A) 28 August 2003 (2003-08-28) page 75, lines 15-21 SEQ ID NO:425, 426: RPI#30350/30361 page 146 page 146 page 116 - page 118; figures 24,25; example 13	1-4, 13-15, 20,21, 24,30,31
MCCAFFREY A.P. ET AL.: "Inhibition of hepatitis B virus in mice by RNA interference" NATURE BIOTECHNOLOGY, vol. 21, no. 6, 1 June 2003 (2003-06-01), pages 639-644, XP008040439 HBVU6no.1 the whole document	
ANDINO R.: "RNAi puts a lid on virus replication" NATURE BIOTECHNOLOGY, vol. 21, no. 6, 1 June 2003 (2003-06-01), pages 629-630, XP002311173 the whole document	
SHLOMAI A. AND SHAUL Y.: "Inhibition of hepatitis B virus expression and replication by RNA interference" HEPATOLOGY, vol. 37, no. 4, April 2003 (2003-04), pages 764-770, XP008040408 the whole document	
COUZIN J.: "Mini RNA molecules shield mouse liver from hepatitis" SCIENCE, vol. 299, 14 February 2003 (2003-02-14), page 995, XP002310940 the whole document	·
	WO 03/070918 A (RIBOZYME PHARMA INC (US) MCSWIGGEN BEIGELMAN MACEJAK ZINNEN PAVCO ET A) 28 August 2003 (2003-08-28) page 75, lines 15-21 SEQ ID NO:425, 426: RPI#30350/30361 page 146 page 116 - page 118; figures 24,25; example 13 MCCAFFREY A.P. ET AL.: "Inhibition of hepatitis B virus in mice by RNA interference" NATURE BIOTECHNOLOGY, vol. 21, no. 6, 1 June 2003 (2003-06-01), pages 639-644, XP008040439 HBVU6no.1 the whole document ANDINO R.: "RNAi puts a lid on virus replication" NATURE BIOTECHNOLOGY, vol. 21, no. 6, 1 June 2003 (2003-06-01), pages 629-630, XP002311173 the whole document SHLOMAI A. AND SHAUL Y.: "Inhibition of hepatitis B virus expression and replication by RNA interference" HEPATOLOGY, vol. 37, no. 4, April 2003 (2003-04), pages 764-770, XP008040408 the whole document COUZIN J.: "Mini RNA molecules shield mouse liver from hepatitis" SCIENCE, vol. 299, 14 February 2003 (2003-02-14), page 995, XP002310940 the whole document

	ation) DOCUMENTS CONSIDERED TO BE RELEVANT Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
Category °	Citation of document, with indication, where appropriate, of the relevant passages	nelevani to daim No.
A	HAMASAKI K. ET AL.: "Short interfering RNA-directed inhibition of hepatitis B virus replication" FEBS LETTERS, ELSEVIER SCIENCE PUBLISHERS, AMSTERDAM, NL, vol. 543, no. 1-3, 22 May 2003 (2003-05-22), pages 51-54, XP004425032 ISSN: 0014-5793 the whole document	
Α .	WILSON J.A. ET AL.: "RNA interference blocks gene expression and RNA synthesis from hepatitis C replicons propagated in human liver cells" PROCEEDINGS OF THE NATIONAL ACADEMY OF SCIENCES OF USA, NATIONAL ACADEMY OF SCIENCE. WASHINGTON, US, vol. 100, no. 5, 4 March 2003 (2003-03-04), pages 2783-2788, XP002300963 ISSN: 0027-8424 the whole document	
A .	MCCAFFREY A.P. ET AL.: "RNA interference in adult mice" NATURE, MACMILLAN JOURNALS LTD. LONDON, GB, vol. 418, no. 6893, 4 July 2002 (2002-07-04), pages 38-39, XP002234152 ISSN: 0028-0836 the whole document	
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International application No. PCT/US2004/019229

Box II Observations where certain claims were found unsearchable (Continuation of item 2 of first sheet)
This International Search Report has not been established in respect of certain claims under Article 17(2)(a) for the following reasons:
Claims Nos.: because they relate to subject matter not required to be searched by this Authority, namely:
Although claims 1-14 and 9-13 are directed to a method of treatment of the human/animal body, the search has been carried out and based on the alleged effects of the compound/composition.
2. Claims Nos.: because they relate to parts of the International Application that do not comply with the prescribed requirements to such an extent that no meaningful International Search can be carried out, specifically:
· ·
3. Claims Nos.: because they are dependent claims and are not drafted in accordance with the second and third sentences of Rule 6.4(a).
Box III Observations where unity of invention is lacking (Continuation of item 3 of first sheet)
This International Searching Authority found multiple inventions in this international application, as follows:
see additional sheet
1. As all required additional search fees were timely paid by the applicant, this International Search Report covers all searchable claims.
As all searchable claims could be searched without effort justifying an additional fee, this Authority did not invite payment of any additional fee.
3. As only some of the required additional search fees were timely paid by the applicant, this International Search Report covers only those claims for which fees were paid, specifically claims Nos.:
4. No required additional search fees were timely paid by the applicant. Consequently, this International Search Report is restricted to the invention first mentioned in the claims; it is covered by claims Nos.: 1-4, 9-15, 18-21, 23-27, 30, 31 all partially
Remark on Protest The additional search fees were accompanied by the applicant's protest. No protest accompanied the payment of additional search fees.

FURTHER INFORMATION CONTINUED FROM PCT/ISA/ 210

This International Searching Authority found multiple (groups of) inventions in this international application, as follows:

1. claims: 1-4, 9-15, 18-21, 23-27, 30, 31 all partially

A method for inhibiting expression of a polynucleotide sequence of hepatitis B virus by means of a double-stranded RNA effector molecule comprising an at least 19 contiguous base pair nucleotide sequence from SEQ ID NO:1. Methods, compositions, polynucleotide sequences, expression constructs and mammalian cells related thereto. A polynucleotide sequence comprising at least 19 contiguous base pair nucleotide sequence from SEQ ID NO:25 or SEQ ID NO:26.

2. claims: 1-4, 9-15, 18-21, 23-27, 30, 31 all partially

A method for inhibiting expression of a polynucleotide sequence of hepatitis B virus by means of a double-stranded RNA effector molecule comprising an at least 19 contiguous base pair nucleotide sequence from SEQ ID NO:2. Methods, compositions, polynucleotide sequences, expression constructs and mammalian cells related thereto. A polynucleotide sequence comprising at least 19 contiguous base pair nucleotide sequence from SEQ ID NO:23 or SEQ ID NO:24.

3. claims: 1-4, 9-15, 18-21, 23-27, 30, 31 all partially

A method for inhibiting expression of a polynucleotide sequence of hepatitis B virus by means of a double-stranded RNA effector molecule comprising an at least 19 contiguous base pair nucleotide sequence from SEQ ID NO:3. Methods, compositions, polynucleotide sequences, expression constructs and mammalian cells related thereto. A polynucleotide sequence comprising at least 19 contiguous base pair nucleotide sequence from SEQ ID NO:19, SEQ ID NO:20, SEQ ID NO:21 or SEQ ID NO:22.

4. claims: 1-4, 9-15, 18-21, 23-27, 30, 31 all partially

A method for inhibiting expression of a polynucleotide sequence of hepatitis B virus by means of a double-stranded RNA effector molecule comprising an at least 19 contiguous base pair nucleotide sequence from SEQ ID NO:4. Methods, compositions, polynucleotide sequences, expression constructs and mammalian cells related thereto. A polynucleotide sequence comprising at least 19 contiguous base pair nucleotide sequence from SEQ ID NO:16 or SEQ ID NO:17.

FURTHER INFORMATION CONTINUED FROM PCT/ISA/ 210

5. claims: 1-4, 9-15, 18-21, 23-27, 30, 31 all partially

A method for inhibiting expression of a polynucleotide sequence of hepatitis B virus by means of a double-stranded RNA effector molecule comprising an at least 19 contiguous base pair nucleotide sequence from SEQ ID NO:5, SEQ ID NO:6, SEQ ID NO:7, SEQ ID NO:8.

Methods, compositions, polynucleotide sequences, expression constructs and mammalian cells related thereto.

A polynucleotide sequence comprising at least 19 contiguous base pair nucleotide sequence from SEQ ID NO:14 or SEQ ID NO:15.

6. claims: 1-4, 9-15, 18-21, 23-25, 30, 31 all partially

A method for inhibiting expression of a polynucleotide sequence of hepatitis B virus by means of a double-stranded RNA effector molecule comprising an at least 19 contiguous base pair nucleotide sequence from SEQ ID NO:9. Methods, compositions, polynucleotide sequences, expression constructs and mammalian cells related thereto.

7. claims: 1-4, 9-15, 18-21, 23-27, 30, 31 all partially

A method for inhibiting expression of a polynucleotide sequence of hepatitis B virus by means of a double-stranded RNA effector molecule comprising an at least 19 contiguous base pair nucleotide sequence from SEQ ID NO:10. Methods, compositions, polynucleotide sequences, expression constructs and mammalian cells related thereto. A polynucleotide sequence comprising at least 19 contiguous base pair nucleotide sequence from SEQ ID NO:18.

8. claims: 5-13, 16-20, 22-25, 30, 31 all partially

A method for inhibiting expression of a polynucleotide sequence of hepatitis C virus by means of a double-stranded RNA effector molecule comprising an at least 19 contiguous base pair nucleotide sequence from SEQ ID NO:11. Methods, compositions, polynucleotide sequences, expression constructs and mammalian cells related thereto.

9. claims: 5-13, 16-20, 22-25, 30, 31 all partially

A method for inhibiting expression of a polynucleotide sequence of hepatitis B virus by means of a double-stranded RNA effector molecule comprising an at least 19 contiguous base pair nucleotide sequence from SEQ ID NO:12. Methods, compositions, polynucleotide sequences, expression constructs and mammalian cells related thereto.

FURTHER INFORMATION CONTINUED FROM PCT/ISA/ 210

10. claims: 28-31 all partially

A polynucleotide sequence comprising at least 19 contiguous base pair nucleotide sequence from SEQ ID NO:27. Expression construct and mammalian cell related thereto. A polynucleotide sequence comprising at least 19 contiguous base pair nucleotide sequence from SEQ ID NO:29, SEQ ID NO:30, SEQ ID NO:31, SEQ ID NO:32, SEQ ID NO:33, SEQ ID NO:34, SEQ ID NO:35, SEQ ID NO:36, SEQ ID NO:37, SEQ ID NO:38, SEQ ID NO:39, SEQ ID NO:40, SEQ ID NO:41, SEQ ID NO:42, SEQ ID NO:43 or SEQ ID NO:44.

11. claim: 28 partially

A polynucleotide sequence comprising at least 19 contiguous base pair nucleotide sequence from SEQ ID NO:28.

International Application No
PCT/US2004/019229

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